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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/560,288	04/27/00	HANLEY E	8151-24A

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HM12/0807

EXAMINER	
KERR, J	

ART UNIT	PAPER NUMBER
1633	10

DATE MAILED: 08/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
09/560,288	Hanley et al.
Examiner	**Art Unit**
Janet M. Kerr	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Jul 26, 2001* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) ☒ they raise the issue of new matter. (See NOTE below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: *see attached.*

4. ☒ Applicant's reply has overcome the following rejection(s):
   None, see attached.

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☒ The a) ☒ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
   See attached.

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

   Claim(s) allowed: *None*

   Claim(s) objected to: _____

   Claim(s) rejected: *10, 11, 13-15, and 18-34*

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

11. ☐ Other:

DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Response to Amendment Submitted After Final

The amendment submitted 7/26/01 will not be entered as the amended claims raise a new matter issue and would require further search and consideration. With regard to the new matter issue, the methods claims, as well as the product-by-process claims, have been amended to include the limitation that the cells required in the therapeutic composition are intervertebral annulus disc cells obtained from a monolayer human intervertebral annulus disc cell culture. There is no support in the specification or the claims as originally filed for obtaining intervertebral annulus disc cells from the monolayer culture. The claims as originally filed, and subsequent amended claims, were directed to obtaining and utilizing intervertebral disc cells which, based on the specification, comprise both annulus and nucleus cell populations. There is no disclosure in the specification of specifically isolating and culturing annulus cells, of a composition of annulus cells prepared by the cell culture method, or treatment of intervertebral disc diseases with the population of annulus cells. As the newly amended claims limit the cell population required in the therapeutic composition, and limit the cell population utilized in the treatment method, the claims would also require a further search and consideration as the cells in the pending claims are directed to intervertebral disc cells (which, when read in light of the specification, encompass both annulus and nucleus cells).

Applicant's arguments filed 7/26/01 have been fully considered but they are not persuasive. It is argued that the specification discusses the use of annulus and nucleus cells in the invention and while annulus cells have been used, it would not matter if there were a few cells from the nucleus region of the disc. It is further asserted by Declarant Gruber that annulus cells were used in the study. These arguments are not persuasive as the specification discloses culturing both annulus and nucleus cells obtained from intervertebral disc tissue (see page 5, lines 8-21) and using the cultured cells in the therapeutic method of treating intervertebral disc disease. There is

no teaching in the specification that only annulus cells were cultured and utilized in the claimed methods.

The references of Walmsley, Taylor *et al.*, Butler, and Errington *et al.* have been reviewed. However, the teachings in the references are not sufficient to overcome the rejections of record. The rejections of record are directed to the types of cells expanded in vitro, the differentiation state of the cells, and the use of these cells in a therapeutic application. In contrast, The teachings of Walmsley, as well as Taylor *et al.*, and Butler are directed to a general review of the development and growth of the intervertebral disc *in situ*. The teachings of Errington *et al.* are directed to the morphological characterization of nucleus and annulus cells. These references do not provide guidance with respect to how to make and use the therapeutic composition such that successful treatment of an intervertebral disc disease is achieved.

With regard to the question of proliferative status of the cells required in the claimed products and methods, it is initially stated that the annulus cells are proliferating cells. It is then asserted that the state of differentiation of the cells are de-differentiated or are differentiated. This assertion is inconsistent with the first statement that the cells are proliferating (there is no evidence of record that the cells which are differentiated are proliferating).

The declaration under 37 CFR 1.132 filed 7/26/01 is insufficient to overcome the rejection of claims 10, 11, 13, 15, and 18-34 based upon 35 U.S.C. 112, first paragraph as set forth in the last Office action for the following reasons. In paragraph 6 of the declaration, it is indicated that the type of disc cells that are cultured *in vitro* are cells from the annulus and that there is detailed discussion and examples (e.g., examples 4 and 5) of the use of annulus cells. This is not persuasive. As stated above, the specification describes a co-culture of annulus and nucleus cells and a use of the co-culture in a therapeutic application. There is no disclosure in the specification of culturing annulus cells alone. In paragraphs 7-9, it is asserted that the cells of the annulus are proliferating cells which secrete extracellular matrix components including type I collagen, type II

collagen, chondroitin sulfate and keratin sulfate (as demonstrated by immunolocalization studies provided in Exhibit B). This argument is not persuasive as Declarant Gruber is arguing limitations not in the claims. There is no recitation in the claims or disclosure in the specification that the cells used for transplantation are in a differentiated state or in a de-differentiated state.

For the reasons of record and the reasons set forth above, the rejections are maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600